In the Claims

The following amendments are made with respect to the claims in the International application PCT/IB2003/003444.

This listing of claims will replace all prior versions and listings of claims in this application.

1 (currently amended). A method of identifying and/or designing and/or modifying and/or optimizing species capable of interacting with a macromolecule, comprising the steps:

a) defining a set of physiological functions and/or properties of said macromolecule and/or said species, said physiological functions and/or properties being based on empirical data, available for said macromolecule and/or said species,

b) identifying a mechanical analogue from the set of physiological functions and/or properties of said macromolecule and/or said species, which mechanical analogue performs a mechanical function that is analogous to the physiological function of said macromolecule and/or species, and which mechanical analogue performs the mechanical function as a whole or which mechanical analogue consists of parts allowing said mechanical analogue to perform its mechanical function, such that each of said parts of said mechanical analogue performs a component of said mechanical function,

c) providing at least one structure of said macromolecule and/or species, said structure being a representation of the arrangement and connectivity of the atoms of said macromolecule and/or said species, in three dimensional space, or said structure being a set of all coordinates of the atoms of said macromolecule and/or species in three dimensional space, said macromolecule and/or species consisting of building blocks, referred to as residues,

d) identifying a group of residues within the structure of said macromolecule and/or species, said group of residues performing a specific component of physiological function of said macromolecule and/or species, or said group of residues performing a part of said physiological function of said macromolecule and/or species, which group of residues are analogous to a part of said mechanical analogue (identified in b) which performs a part of said mechanical function, said group of residues being referred to as a macromolecule architectural component (MAC), said component of physiological function of said macromolecule having its counterpart in at least one part of the mechanical analogue,

identified in b), which mechanical analogue part performs an analogous component of mechanical function in said mechanical analogue,

e) repeating step d) as many times as necessary until all macromolecule architectural components are identified which are necessary for said macromolecule and/or species to perform its physiological function,

f) representing each MAC identified in step d) by a geometrical shape, which shape approximates the dimensions of said MAC,

g) assigning the approximate dimensions to each geometrical shape of step f), thereby defining the coordinates and dimensions of each MAC,

h) calculating the centres of mass and inter-MAC angles using the coordinates of each MAC, and

i) parameterising the identification/design/modification/optimization of species capable of interacting with said macromolecule, by using the inter MAC-angles, centres of mass and the dimensions of the MACs.

2 (currently amended). The method according to claim 1, further comprising the steps of:

j) physically providing/designing/modifying/optimizing a species suspected of interacting with said macromolecule, the identity of said species being based on information retrieved from performing steps a) - i) on said species as well as on said macromolecule,

k) physically providing said macromolecule, and

l) physically mixing said species and said macromolecule and measuring an interaction.

3 (currently amended). The method according to claim 2, wherein the order of steps j) and k) is ~~reverse~~ reversed.

4 (currently amended). The method according to ~~any of claims 1—3~~ claim 1, wherein said macromolecule is selected from the group ~~comprising~~ consisting of proteins, nucleic acids, carbohydrates, lipids and fats.

5 (currently amended). The method according to claim 4, wherein said macromolecule is selected from the group ~~comprising~~ consisting of A-DNA, B-DNA, Z-DNA, RNA~~, in particular t-RNA, r-RNA and m-RNA,~~ ribozymes, proteins, protein complexes, peptides, peptidoglycans, carbohydrates, lipids and fats.

6 (currently amended). The method according to ~~any of the foregoing claims~~ claim 1, wherein said species is selected from the group ~~comprising~~ consisting of proteins, peptides, nucleic acids, carbohydrates, lipids, fats, non-protein co-factors, small-molecule-compounds, radicals, ions and macromolecule associated water molecules.

7 (currently amended). The method according to claim 6, wherein said small-molecule-compounds have a molecular mass in the range of 150-1300~~, preferably 200-900, more preferably 300-600~~.

8 (currently amended). The method according to ~~any of the foregoing claims~~ claim 1, wherein the approximate dimensions assigned in step g) are in Ångstroms.

9 (currently amended). The method according to ~~any of the foregoing claims~~ claim 1, wherein said macromolecule is pictorially represented using inter-MAC angles, centres of mass of said MACs and said dimensions of said MACs.

10 (original). The method according to claim 9, wherein the pictorial representation is by means of the geometrical shapes identified in step f), whereby each MAC is represented independently by a geometrical shape, such that the geometrical shape of one MAC may be the same as that of another MAC or they may be different.

11 (currently amended). The method according to ~~any of the foregoing claims~~ claim 1, wherein in the steps d) to f) the MACs are construed by referring to said structure or to said set of coordinates provided in step c), to assign a geometric shape and dimensions, based on said empirical data.

12 (currently amended). The method according to ~~any of the foregoing claims~~ claim 1, wherein the macromolecule architectural component identified in d) comprises residues which are more than 2Å apart.

13 (currently amended). The method according to ~~any of the foregoing claims~~ claim 1, wherein the macromolecule architectural component occurs within a part of the tertiary structure of the macromolecule that is well defined, as judged by X-ray-data and/or NMR-data and/or homology modeling studies.

14 (original). The method according to claim 13, wherein said macromolecule is a protein.

15 (original). The method according to claim 14, wherein the macromolecule architectural component occurs within a part of the tertiary structure of the protein, the Cα-atoms of which have B-factors in the range of from $2Å^2$-$200Å^2$.

16 (currently amended). The method according to ~~any of~~ claims 13 ~~or 15~~, wherein the macromolecule architectural component occurs in a region of the tertiary structure of the macromolecule the backbone atoms of which have a root mean square deviation (RMSD) in the range of from 0.05 Å -4.0Å.

17 (currently amended). The method according to ~~any of the foregoing~~ claims 1, wherein said macromolecule architectural component(s) is (are independently) represented by a geometrical shape, said shape being selected from the group consisting of ~~comprising~~ planes, parallelepipeds, cubes, cylinders, spirals, rings, tori, ellipsoids, balls and any combination thereof.

18 (original). The method according to claim 17, wherein said geometrical shape represents/is similar to a mechanical part of a machine, such as planks/sheets, springs, tubes, screws, bolts, nuts, rivets, bushings, bearings and other components used for manufacturing a machine or component of a machine.

19 (currently amended). The method according to ~~any of claims 17-18~~ claim 17, wherein the geometricial shape selected for a MAC is a plane.

20 (original). The method according to claim 19, wherein a macromolecule architectural component is represented by a difference vector matrix A, wherein

'A'	=	$[(x_i - \langle x \rangle)(y_i - \langle y \rangle)(z_i - \langle z \rangle)]$
(x_i, y_i, z_i)	=	[X, Y, Z] coordinates of the central atom of each residue in the MAC, e.g. of the Cα atom, in the PAC
$(\langle x \rangle, \langle y \rangle, \langle z \rangle)$	=	$(\Sigma x_i/n, \Sigma y_i/n, \Sigma z_i/n)$
n	=	Number of central atoms of each residue in each MAC, e.g. of Cα atoms in each PAC.

21 (original). The method according to claim 20, wherein said difference vector matrix A is solved to yield a singular vector which represents the direction cosine of the vector which is normal to the best-fitting plane of the given coordinates of the macromolecule architectural component.

22 (currently amended). The method according to ~~any of claims 17-18~~ claim 17, wherein the geometrical shape selected for a MAC is a cylinder or a spiral.

23 (original). The method according to claim 22, wherein a directional vector intersecting with the longitudinal axis of said cylinder or spiral is calculated.

24 (original). The method according to claim 23, wherein said calculation occurs by the method of besection of vectors.

25 (currently amended). The method according to ~~any of the foregoing claims~~ claim 1, wherein the physiological functions and/or properties of the macromolecule are selected

from the group ~~comprising~~ consisting of oxidoreductase, transferase, hydrolase, lyase, isomerase and ligase.

26 (currently amended). The method according to claim 25, wherein the physiological functions and/or properties of the macromolecule are selected from the group ~~comprising~~ consisting of protease, kinase, phosphorylase, DNAase, RNAase, lipase and polymerase.

27 (currently amended). The method according to ~~any of claims 1-24~~ claim 1, wherein the physiological functions and/or properties of the macromolecule are selected from the group ~~comprising~~ consisting of regulatory function in cell metabolism, regulatory function in transcription and/or translation, regulatory function in signal transduction pathways, structural function, storage function, motility function, transport function, and recognition function.

28 (currently amended). The method according to ~~any of claims 2-27~~ claim 2, wherein the measurement of an interaction between the species suspected of interacting with said macromolecule and said macromolecule, in step 1), occurs by UV-vis-absorption spectroscopy, fluorescence spectroscopy, circular dichroism, NMR-spectroscopy, surface plasmon resonance spectroscopy, gelfiltration, ultracentrifugation, viscometry, electrophoresis, and/or any combination of the aforementioned techniques.

29 (currently amended). A species and/or macromolecule identified/designed/modified/optimized by ~~the method according to any of claims 1-28~~ a method of identifying and/or modifying and/or optimizing species capable of interacting with a macromolecule, comprising the steps:

a) defining a set of physiological functions and/or properties of said macromolecule and/or said species, said physiological functions and/or properties being based on empirical data, available for said macromolecule and/or said species,

b) identifying a mechanical analogue from the set of physiological functions and/or properties of said macromolecule and/or said species, which mechanical analogue performs a mechanical function that is analogous to the physiological function of said macromolecule and/or species, and which mechanical analogue performs the mechanical

function as a whole or which mechanical analogue consists of parts allowing said mechanical analogue to perform its mechanical function, such that each of said parts of said mechanical analogue performs a component of said mechanical function,

c) providing at least one structure of said macromolecule and/or species, said structure being a representation of the arrangement and connectivity of the atoms of said macromolecule and/or said species, in three dimensional space, or said structure being a set of all coordinates of the atoms of said macromolecule and/or species in three dimensional space, said macromolecule and/or species consisting of building blocks, referred to as residues,

d) identifying a group of residues within the structure of said macromolecule and/or species, said group of residues performing a specific component of physiological function of said macromolecule and/or species, or said group of residues performing a part of said physiological function of said macromolecule and/or species, which group of residues are analogous to a part of said mechanical analogue (identified in b) which performs a part of said mechanical function, said group of residues being referred to as a macromolecule architectural component (MAC), said component of physiological function of said macromolecule having its counterpart in at least one part of the mechanical analogue, identified in b), which mechanical analogue part performs an analogous component of mechanical function in said mechanical analogue,

e) repeating step d) as many times as necessary until all macromolecule architectural components are identified which are necessary for said macromolecule and/or species to perform its physiological function,

f) representing each MAC identified in step d) by a geometrical shape, which shape approximates the dimensions of said MAC,

g) assigning the approximate dimensions to each geometrical shape of step f), thereby defining the coordinates and dimensions of each MAC,

h) calculating the centres of mass and inter-MAC angles using the coordinates of each MAC, and

i) parameterising the identification/design/modification/optimization of species capable of interacting with said macromolecule, by using the inter MAC-angles, centres of mass and the dimensions of the MACs.

30 (currently amended). A graphical representation of a ~~macromolecule and/or species, as defined in any of the foregoing claims, generated by the method according to the foregoing claims~~ species and/or macromolecule identified/designed/modified/optimized by a method of identifying and/or modifying and/or optimizing species capable of interacting with a macromolecule, comprising the steps:

a) defining a set of physiological functions and/or properties of said macromolecule and/or said species, said physiological functions and/or properties being based on empirical data, available for said macromolecule and/or said species,

b) identifying a mechanical analogue from the set of physiological functions and/or properties of said macromolecule and/or said species, which mechanical analogue performs a mechanical function that is analogous to the physiological function of said macromolecule and/or species, and which mechanical analogue performs the mechanical function as a whole or which mechanical analogue consists of parts allowing said mechanical analogue to perform its mechanical function, such that each of said parts of said mechanical analogue performs a component of said mechanical function,

c) providing at least one structure of said macromolecule and/or species, said structure being a representation of the arrangement and connectivity of the atoms of said macromolecule and/or said species, in three dimensional space, or said structure being a set of all coordinates of the atoms of said macromolecule and/or species in three dimensional space, said macromolecule and/or species consisting of building blocks, referred to as residues,

d) identifying a group of residues within the structure of said macromolecule and/or species, said group of residues performing a specific component of physiological function of said macromolecule and/or species, or said group of residues performing a part of said physiological function of said macromolecule and/or species, which group of residues are analogous to a part of said mechanical analogue (identified in b) which performs a part of said mechanical function, said group of residues being referred to as a macromolecule architectural component (MAC), said component of physiological function of said macromolecule having its counterpart in at least one part of the mechanical analogue, identified in b), which mechanical analogue part performs an analogous component of mechanical function in said mechanical analogue,

e) repeating step d) as many times as necessary until all macromolecule architectural components are identified which are necessary for said macromolecule and/or species to perform its physiological function,

f) representing each MAC identified in step d) by a geometrical shape, which shape approximates the dimensions of said MAC,

g) assigning the approximate dimensions to each geometrical shape of step f), thereby defining the coordinates and dimensions of each MAC,

h) calculating the centres of mass and inter-MAC angles using the coordinates of each MAC, and

i) parameterising the identification/design/modification/optimization of species capable of interacting with said macromolecule, by using the inter MAC-angles, centres of mass and the dimensions of the MACs.